AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application:

Listing of Claims:

1-57 (Cancelled)

58. (Currently Amended) A device for identifying at least one differentially spliced gene product, wherein said device comprises ~~product comprising a support material and a plurality of different nucleic acid molecules, wherein~~

a solid support material and single-stranded oligonucleotides of between 5 and 100 nucleotides in length ~~the nucleic acid molecules are~~ attached to said ~~the~~ support material,

wherein said oligonucleotides comprise at least a first and a second oligonucleotide molecule arranged serially on the support material,

wherein said first oligonucleotide molecule comprises ~~the nucleic acid molecules comprise~~ a first sequence that ~~which~~ is complementary to and specific for an exon or an intron of a first gene, and wherein said first sequence ~~and which~~ corresponds to a region of variability in at least one product of said first gene due to differential splicing ~~of said gene~~, and

wherein said second oligonucleotide molecule ~~said product~~ comprises a second sequence that is complementary to and specific for an exon-exon or exon-intron junction region of said first gene, and wherein said second sequence corresponds to a region of variability in at least one product of said first gene due to differential splicing ~~at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene~~,

said device ~~product~~ allowing, when contacted with a sample containing at least one nucleic acid molecule ~~acids~~ under conditions allowing hybridisation to occur, the determination of the presence or absence of said differentially spliced gene product ~~exon or intron of said gene in said sample~~.

59-62 (Cancelled)

63. (Currently Amended) The device ~~product~~ of claim 58 ~~61 or 62~~, wherein said first and second oligonucleotide molecules are available from a ~~the identification step (a) is based upon~~ compilation of published sequences or sequence information from at least one database ~~databases~~.

64. (Cancelled)

65. (Currently Amended) The device ~~product~~ of claim 58 ~~or 59~~, wherein the support material is selected from the group consisting of a filter, a membrane and a chip.

66. (Currently Amended) The device ~~product~~ of claim 58 ~~or 59~~, wherein said single-stranded oligonucleotides ~~the nucleic acid molecules~~ are RNA or DNA ~~comprise cDNA~~ molecules ~~fragments~~.

67. (Cancelled)

68. (Currently Amended) The device ~~product~~ of claim 58 ~~67~~, wherein said single-stranded oligonucleotides comprise ~~the nucleic acid molecules comprise single-stranded~~ oligonucleotides of less than 50 nucleotides ~~between 5 and 100 bases~~ in length.

69. (Currently Amended) The device ~~product~~ of claim 58 ~~or 59~~, wherein said single-stranded oligonucleotides ~~the nucleic acid molecules~~ are specific for ~~of~~ alternative splicings representative of a cell or tissue in a given pathological condition.

70. (Currently Amended) The device ~~product~~ of claim 69, wherein said single-stranded oligonucleotides ~~the nucleic acid molecules~~ are specific for ~~of~~ alternative splicings representative of a tumor cell or tissue.

71. (Currently Amended) The device ~~product~~ of claim 69, wherein said single-stranded oligonucleotides ~~the nucleic acid molecules~~ are specific for ~~of~~ alternative splicings representative of a cell or tissue undergoing apoptosis.

72. (Currently Amended) The device of claim 58, where said device is useful to evaluate ~~A product for evaluating~~ the toxicity of a compound or treatment to a cell, tissue, or organism by determining the presence or absence of said differentially spliced gene product in a sample treated with said compound or treatment~~, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample~~.

73-79 (Cancelled)

80. (Currently Amended) The device of claim 58, where said device is useful to evaluate ~~A product for evaluating~~ the therapeutic efficacy of a compound to a cell, tissue, or organism by determining the presence or absence of said differentially spliced gene product in a sample from said cell, tissue, or organism~~, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing~~

~~hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample~~.

81-87 (Cancelled)

88. (Currently Amended) The device of claim 58, where said device is useful to evaluate ~~A product for evaluating~~ the responsiveness of a subject to a compound or treatment by determining the presence or absence of said differentially spliced gene product in a sample from said subject exposed to said compound or treatment~~, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell from a responsive subject treated by a reference therapeutic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample~~.

89-90 (Cancelled)

91. (Currently Amended) A device ~~product~~ comprising, immobilized on a support material, a nucleic acid library comprising a plurality of nucleic acid molecules of between 5 and 100 nucleotides in length serially arranged on said support material, wherein each of said nucleic acid molecules comprises a sequence that is complementary to and specific for ~~corresponding to~~ a portion of a gene which is differentially spliced between two physiological conditions of a cell or tissue, said library being enriched for said nucleic acid molecules.

92. (Currently Amended) A device ~~product~~ comprising, immobilized on a support material, a nucleic acid library comprising a plurality of oligonucleotide pairs, each pair of oligonucleotides comprising a first and a second oligonucleotide of between 5 and 100 nucleotides in length serially arranged on said support material, wherein said first and second oligonucleotides of each of said pairs comprise sequences that are complementary to and specific for ~~corresponding to~~ differentially spliced forms of a gene, said library being enriched for said pairs.

93. (Currently Amended) A device ~~product~~ comprising, immobilized on a support material, a microorganism library comprising microorganisms transformed by a nucleic library of claim 91.

94. (Currently Amended) A method of producing a device ~~product~~ comprising a support material and single-stranded oligonucleotide of between 5 and 100 nucleotides in length attached to said solid support material ~~a plurality of different nucleic acid molecules~~, wherein said method comprises:

(a) providing said ~~a plurality of at least two cDNA molecules or single-stranded~~ oligonucleotides, wherein said oligonucleotides comprise at least a first and a second oligonucleotide molecule, ~~comprising a sequence which is complementary to and specific for distinct exons or introns of a gene or RNA and which correspond to a region of variability due to differential splicing of said gene or RNA, and~~

wherein said first oligonucleotide molecule comprises a first sequence that is complementary to and specific for an exon or an intron of a first gene, and wherein said first sequence corresponds to a region of variability in at least one product of said first gene due to differential splicing, and

wherein said second oligonucleotide molecule comprises a second sequence that is complementary to and specific for an exon-exon or exon-intron junction region of said first gene, and wherein said second sequence corresponds to a region of variability in at least one product of said first gene due to differential splicing; and

(b) arranging and immobilizing said oligonucleotides serially on said ~~plurality of cDNA molecules or single-stranded oligonucleotides to a~~ support material,

said device ~~product~~ allowing, when contacted with a sample containing at least one nucleic acid molecule ~~nucleic acids~~ under conditions allowing hybridisation to occur, the determination of the presence or absence of at least one differentially spliced gene product ~~said exon or intron of said gene or RNA in said sample~~.

95-96 (Cancelled)

97. (Currently Amended) The method of claim 94, wherein said first or second oligonucleotide molecule is obtained by a method comprising: ~~providing said plurality of different nucleic acid molecules comprising cDNA molecules comprises:~~

(a) identifying at least two different oligonucleotides corresponding to a differentially spliced domain of a gene, wherein said differentially spliced domain is characteristic of a physiopathological condition, and

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain or a junction region formed by the splicing or absence of splicing of said domain, and

~~(a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown, and~~

~~(b) identifying or cloning, from the hybrids formed in (a), a population of nucleic acid molecules comprising an unpaired region, said cloned or identified nucleic acid molecules comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples~~.

98. (Currently Amended) The method of claim 97 94, wherein the identification step (a) ~~providing said plurality of different nucleic acid molecules comprising single-stranded~~

~~oligonucleotides~~ comprises:

i) hybridizing a plurality of different RNA or cDNA molecules derived from a first sample, wherein the composition or sequence of the RNA or cDNA molecules is at least partially unknown, with a plurality of different cDNA molecules derived from RNA molecules of a second sample, wherein the composition or sequence of the cDNA molecules is at least partially unknown; and

ii) identifying, from the hybrids formed in i), a population of nucleic acid molecules comprising an unpaired region, wherein said unpaired region corresponds to a region of a gene that is differentially spliced between said first and second sample

~~(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,~~

~~(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain, and~~

~~(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition~~.

99. (Currently Amended) The method of claim 94, wherein said first and second oligonucleotide molecules are obtained from a compilation of published sequences or sequence information from databases ~~The method of claim 95, wherein providing said plurality of different nucleic acid molecules comprising single-stranded oligonucleotides comprises:~~

~~(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,~~

~~(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and~~

~~(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition~~.

100. (Previously Presented) The method of claim 94, wherein the support material is selected from a filter, a membrane, and a chip.

101. (Currently Amended) The method of claim 94, wherein said single-stranded oligonucleotides ~~the cDNA molecules or oligonucleotides~~ are specific for ~~of~~ alternative splicings representative of a cell or tissue in a given pathological condition.

102. (Currently Amended) The method of claim 101, wherein said single-stranded oligonucleotides ~~the cDNA molecules or oligonucleotides~~ are specific for ~~of~~ alternative splicings representative of a tumor cell or tissue.

103. (Currently Amended) The method of claim 101, wherein said single-stranded oligonucleotides ~~the cDNA molecules or oligonucleotides~~ are specific for ~~of~~ alternative splicings representative of a cell or tissue undergoing apoptosis.

104. (New) The method of claim 94, wherein said single-stranded oligonucleotides comprise oligonucleotides of less than 50 nucleotides in length.

105. (New) The device of claim 58, wherein said device allows the determination of the presence or absence of two or more differentially spliced gene products of said first gene.

106. (New) The device of claim 58, wherein said device allows the determination of the presence or absence of one or more differentially spliced gene products of two or more genes.